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PATENT
Attorney Docket **056707-5009-01**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Gregory M. Glenn *et al.***	)	
U.S. Application No. **10/633,626**	)	Group Art Unit: **1644**
Filed: **August 5, 2003**	)	Examiner: **Yunsoo Kim**
For: **Dry Formulation for Transcutaneous Immunization**	)	

DECLARATION UNDER 37 C.F.R. § 1.132

I, the undersigned, Robert Seid Jr., do hereby declare that:

1. I am a citizen of the United States, residing at 913 Beacon Square Court, Apt 349, Gaithersburg, MD 20878.

2. I have been awarded Doctor of Philosophy in Chemistry from Boston University, Boston, MA. I did my did my postdoctoral training as a Staff Fellow at Bureau of Biologics (now called the Center of Biologics Evaluation and Research, Food and Drug Administration) at Rockville, MD.

3. I have been employed by Iomai Corporation, since August 1, 2005 and I am presently the Vice President of Formulations at Iomai Corporation. During my employment at Iomai Corporation, I have been engaged in research and development in the area of developing vaccine patches for transcutaneous immunization.

4. I am familiar with the specification and pending claims of U.S. Patent Application No. 10/633,626. I have reviewed the Office Action, dated January 3, 2007. For the reasons stated below, I do not believe that the presently claimed invention is an obvious variant of the

inventions claimed in copending U.S. Applications: 10/790,715; 11/109,948; 11/334,349; and 11/514,462.

Comparison of the Claims in the Applications

The copending U.S. Applications 10/790,715; 11/109,948; and 11/334,349 disclose methods of inducing an immune response by administering a formulation to the skin of a subject. However, the copending applications do not teach or suggest dry formulations for inducing an immune response. Moreover, the claims of the copending applications are not directed to methods of inducing an immune response using a dry formulation. In contrast, the present application discloses methods of inducing an immune response by administering a dry formulation comprising an antigen and an adjuvant to the skin of a subject to induce an immune response.

Background of the Claimed Invention of the Present Application

Prior to the present invention, formulations used by Iomai to induce immune responses transcutaneously were "wet" formulations. Iomai commonly used "wet" patches in preclinical studies to establish that a specific vaccine antigen can be delivered to the skin to induce a robust immune response. The success of wet patches in eliciting immune responses transcutaneously has prompted Iomai scientists to develop a "dry" patch approach for vaccine delivery. A dry patch format (a patch containing a dry formulation) is appealing in terms of ease of use in a clinical setting (*i.e.,* less manipulative steps required for administration), and in terms of a reduction of the steps involved for commercial scale manufacturing. A vaccine antigen in dry patch format is also appealing because one would expect the "dry" patch to exhibit a better stability profile once the bulk water has been removed from it.

Delivery of Antigens: Wet Formulation versus Dry Formulation

However, in terms of delivery, one would not expect a patch containing a dry formulation to transcutaneously deliver antigens any better than a patch containing a wet formulation. Intuitively, one would think that for transcutaneous delivery, a patch containing a wet formulation has inherent advantages over a patch with a dry formulation. For instance, antigens need to be solubilized in the patch prior to transport through the outer layers of the skin and into

the skin. A wet formulation on a patch would already have "solubilized" antigens, while a dry formulation on a patch would only have "unsolubilized" antigens. Also, in a patch containing a wet formulation, the water serves as a medium to facilitate Brownian motion, thus, allowing the solubilized antigen molecules to readily diffuse across the patch, through the outer layers of the skin, and into the skin. With a patch containing a dry formulation, there is less movement of the antigen molecules – one can picture the antigens as being entrapped or suspended in the solid patch formulation matrix. Accordingly, one would not expect a patch containing a dry formulation to transcutaneously deliver antigens into the skin to induce an immune response that is enhanced as compared to the immune response induced by a patch containing a wet formulation.

Clinical Trial

Iomai performed a clinical trial to assess the effect of a patch containing a wet formulation ("wet" patch) and a patch containing a dry formulation ("dry" patch). Each of the patches contained 50μg of heat-labile enterotoxin of E. coli (LT). A total of 160 human subjects was randomized to receive either a "wet" or "dry" LT patch. Subjects were immunized twice, at Day 0 (D0) and Day 21 (D21) (three weeks apart), and sera were collected on Day 7, D14, D21, D28, D35, and D42, for determination of LT IgG and LT IgA titers.

Clinical Trial Results and Surprise Finding

Factorial analysis using LT IgG titers and fold rise (ratio to baseline titers) indicated that the dry patch produced higher titers and fold ratios from Day 14 through Day 42 as shown in Figure 1. The dry patch produced statistically significantly higher titers and fold ratios of LT IgA than did the wet patch at all time points from Day 14 onward.

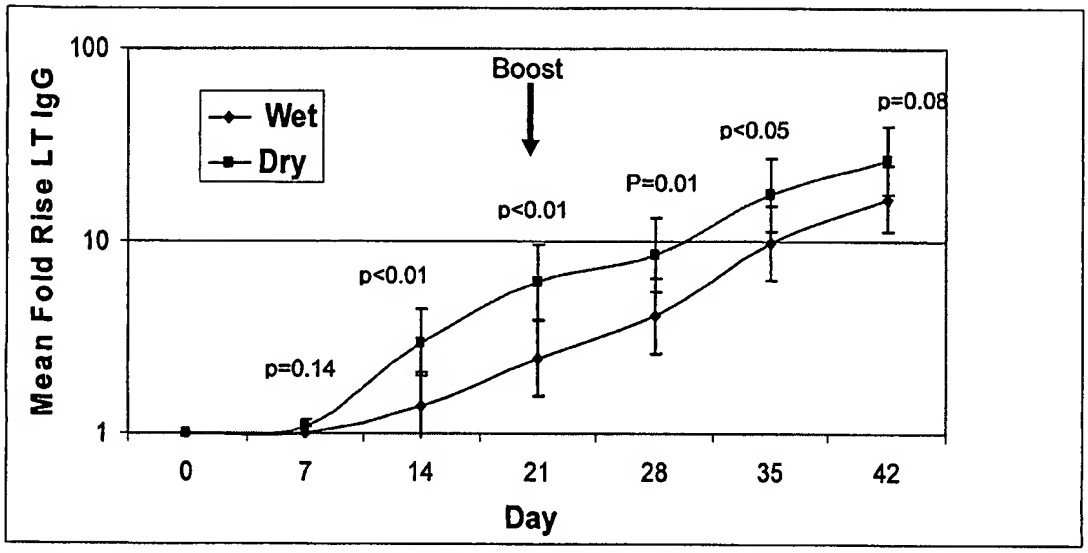

Figure 1. Human subjects received both a "wet" or "dry" patch containing 50μg LT on Day 0 and Day 21. LT IgG were measured on D7, 14, 21, 28, 35, and 42 and compared to baseline titers. The mean fold rise in LT IgG is indicated by the red and blue lines for the "dry" and "wet" patch, respectively.

As discussed above, the scientists at Iomai could not predict that a dry patch would induce an immune response that is greater than the immune response induced by a wet patch. The results of the clinical trial indicating enhanced delivery/immune response using the dry patch shown in Figure 1 could not be predicted. The LT IgG and LT IgA titers and fold ratios clearly showed that the dry patch was better than the wet patch, and that the difference was significant.

5. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: May 2, 2007

By: Robert Seid, Jr.

Robert Seid Jr.